

PATENT  
09/888,309  
Docket 090/002

AMENDMENTS TO THE SPECIFICATION

*Amend the paragraph from page 18, line 38 to page 19, line 7 as follows:*

Certain tissue-specific markers listed in this disclosure or known in the art can be detected by immunological techniques — such as flow immunocytochemistry for cell-surface markers, immunohistochemistry (for example, of fixed cells or tissue sections) for intracellular or cell-surface markers, Western blot analysis of cellular extracts, and enzyme-linked immunoassay, for cellular extracts or products secreted into the medium. The expression of tissue-specific gene products can also be detected at the mRNA level by Northern blot analysis, dot-blot hybridization analysis, or by reverse transcriptase initiated polymerase chain reaction (RT-PCR) using sequence-specific primers in standard amplification methods. Sequence data for the particular markers listed in this disclosure can be obtained from public databases such as GenBank (~~URL~~ [www.ncbi.nlm.nih.gov/80/entrez](http://www.ncbi.nlm.nih.gov/80/entrez)). Expression of tissue-specific markers as detected at the protein or mRNA level is considered positive if the level is at least 2-fold, and preferably more than 10- or 50-fold above that of a control cell, such as an undifferentiated pPS cell, a fibroblast, or other unrelated cell type.

*Amend the paragraph from lines 32-37 on page 6 as follows:*

**Figure 4** is a reproduction of a fluorescence micrograph, showing neuronal cells obtained by direct differentiation of ES cells on a solid substrate using a mixture of differentiation factors. The three fields shown were all taken from treatments that comprised neurotrophins and the ~~TNF- $\beta$~~  TGF- $\beta$  superfamily antagonists noggin and follistatin. A number of cells are seen that have neuronal processes and stain for the neuronal marker  $\beta$ -tubulin-III. The proportion of MAP-2 positive cells that were also positive for tyrosine hydroxylase (a marker for dopaminergic neurons) was as high as ~15%.

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*Amend the paragraph from lines 16 to 23 on page 22 as follows:*

The use of microarray in analyzing gene expression is reviewed generally by Fritz et al Science 288:316, 2000; "Microarray Biochip Technology", M. Schena ed., Eaton Publishing Company; "Microarray analysis", Gwynne & Page, Science (Aug. 6, 1999 supplement); Pollack et al., Nat Genet 23:41, 1999; Gerhold et al., Trends Biochem. Sci. 24:168, 1999; and at the website entitled "Gene Chips (DNA Microarrays)" ~~by L. Shi at the Internet URL www.Gene-Chips.com by~~ Leming Shi, Ph.D. Systems and reagents for performing microarray analysis are available commercially from companies such as Affymetrix, Inc., Santa Clara CA; Gene Logic Inc., Columbia MD; HySeq Inc., Sunnyvale CA; Molecular Dynamics Inc., Sunnyvale CA; Nanogen, San Diego CA; and Synteni Inc., Fremont CA (acquired by Incyte Genomics, Palo Alto CA).